

REMARKS/ARGUMENTS

Claims 1-68 are currently pending in this application. Claims 25, 26 and 27 are independent claims, with all other claims depending from either claim 25, 26 or 27. Claim 55 is hereby amended to specify volumetric flow, and claim 54 is amended to specify that flow conditions in the blood separation system and in collection lines are constant to within 10% of the volumetric flow. Support for these amendments can be found on page 23 of the specification, lines 22-29. All of claims 1-68 are rejected by the Examiner in the Office Action mailed September 12, 2006.

Claim Rejections – 35 USC §112

Claims 54 and 55 are rejected under 35 USC §112, second paragraph. The claims refer to a quasi-steady state flow constant to within 10%, however, do not state specifically what type of flow. The Examiner assumed the 10% referred to volumetric flow and examined the claim on its merits. Claims 54 and 55 are hereby amended to specify volumetric flow. In light of this amendment, this rejection should be withdrawn.

Claim Rejections – 35 USC §102

The Examiner has rejected claims 1, 2, 11, 12, 14-15, 17-22, 25-27, 40, 42-45, 47-50 and 67 under 35 USC §102(b) as being anticipated by U.S. Patent 6,179,801 (Holmes et al.). Holmes discloses a blood processing system and method, specifically a system and method for apheresis.

Claims 25-27 of the present application recite methods of processing blood wherein the total blood volume of the donor is used to determine the removal rate of blood (claim 25), the return rate of blood (claim 26), or both (claim 27). The Examiner rejects claims 25-27 by asserting that Holmes discloses the removal of blood via inlet pump 1030 and the return rate of blood via return pump 1090 according to a predetermined protocol stored in the blood component separation device which operates, in part, on total blood volume of the donor. Therefore, the Examiner

concludes that Holmes discloses the method of claims 25-27. Applicants respectfully traverse.

The system disclosed in Holmes includes a step of calculating the donor's total blood volume which can be used to determine various parameters associated with the apheresis procedure or in the estimation of the number of blood components to be collected (column 56, line 61, to column 57, line 2). It should be noted, however, that Holmes does not disclose what parameters are determined using total blood volume of the donor or how total blood volume is used to modify the apheresis procedure. Specifically, Holmes does not disclose or teach that the removal rate or return rate of blood are controlled or adjusted based on the total blood volume of the donor, as provided in the rejected claims.

The Holmes apparatus uses a pressure sensor 1200 to sense the pressure in both the blood removal tubing 22 and the blood return tubing 24 during operation (column 20, lines 39-43). The output signal of the pressure transducer 1224 is employed to control the operation of the blood inlet pump 1030 and the blood return pump 1090 during operation (column 21, lines 9-12). The monitored pressure changes are communicated to the blood component separation device 6 which in turn controls blood inlet pump 1030 and return pump 1090 so as to maintain fluid pressures within predetermined ranges during blood removal and blood return submodes (column 27, lines 39-44). A desirable range is set forth of about 30 to 300 milliliters/minute through blood return loop 192 utilizing return pump 1090, and a volume transfer operating range of about 20 to 140 milliliters/minute through blood inlet tubing loop 132 utilizing inlet pump 1030 (column 28, lines 54-59). Additional limits for stopping the pumps when excessive negative or positive pressure limits are detected are also given (column 28, lines 59-67). The Holmes patent teaches nothing, however, about controlling the flow rates or pressure limits based on the total blood volume of the donor. In fact, in the portion of the Holmes reference cited by the Examiner (column 27, lines 15-25), the "predetermined protocol" requires only that the volume transfer rate of the return blood

through return blood tubing loop 192 should be greater than the volume transfer rate through blood inlet tubing loop 132 (column 27, lines 15-25 and column 28, lines 54-59). This predetermined protocol is not based in any way on the removal or return blood flow on the basis of the donor's total blood volume.

The only mention of total blood volume in Holmes is found at column 56, line 61 through column 57, line 2, which states: "The donor/patient's 4 total blood volume may be utilized in the determination of various parameters associated with the apheresis procedure and/or in the estimation of the number of blood components which are anticipated to be collected in the procedure." Estimations of blood products, such as estimated platelets or plasma to be recovered, are made using total blood volume, time of donation, hematocrit, and platelet pre-count (column 57 and Figure 35), with time of donation being a parameter that may be varied based on total blood volume. However, this passage does not teach or suggest that the donor's total blood volume can be used to alter the blood removal or return rate as recited in claims 25-27. Further, Applicants assert that this concept is outside the grasp a person of ordinary skill in the art at the time of the invention. Accordingly, Applicants assert this teaching is insufficient to derive the limitations of claims 25-27 from this general passage, or anywhere else in Holmes, without improperly using the disclosure of the present invention.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)." (See MPEP 2131.) Because the Examiner cannot point to any language in Holmes that teaches the removal flow rate or return flow rate being derived from the total blood volume of the donor, this reference cannot anticipate claims 25-27 and the rejection under 35 USC §102 should be withdrawn. Since independent claims 25-27 are not anticipated by Holmes, the remaining claims which depend from these claims also are not anticipated.

The Examiner makes additional rejections to the dependent claims as being anticipated by Holmes. Although Applicants believe Holmes does not anticipate the claims for the reasons stated above, additional grounds for allowance are also offered in support of the dependent claims. Claim 1 and claim 23 recite methods comprising the step of systemically varying or systemically decreasing the return flow rate. The Examiner has rejected claim 1 and claim 23 asserting that Holmes discloses an apheresis system 6 which varies the flow rates based on a predetermined operating scheme (column 27, lines 15-25 and column 56, lines 60-67). Since the blood processing system controls the variations, the Examiner considers the adjusted flow rates to be "systemic" variations. Applicants traverse this rejection because the Examiner has failed to interpret the claims according to the definitions provided in the specification. Page 19, lines 9-12, of the specification defines "systemically varying" as meaning "substantially linear variations, exponential variations, logarithmic variations, quadratic variations." Each of these terms is also expressly defined on pages 16-18 of the specification. Thus, the terms "systemically varying" and "systemically decreasing" do not mean variations controlled by the apheresis system as interpreted by the Examiner, but instead refer to variations that are substantially linear, exponential, logarithmic or quadratic.

Applicants can be their own lexicographers and are free to define "systemically" however they want as long as the term is not given meaning repugnant to the usual meaning of the term (MPEP 608.01(o)). The Examiner's adoption of another definition of "systemically" cannot be sustained in view of the express language of the specification. The rejections of claims 1 and 23 under 35 USC §102 should therefore be withdrawn because the Examiner has failed to show that Holmes varies the return flow rate in a substantially linear, exponential, logarithmic or quadratic manner as required by the specification. Claims 2, 11, 12, 14-15 and 17-22 ultimately depend from claim 1 and therefore incorporate the "systemically varying" limitation. Accordingly, these claims also are not anticipated.

Similarly, the Examiner also rejects claim 2 asserting that the return pump in Holmes is stopped after the completion of the return time. According to the Examiner, this stoppage represents a decrease in the return flow rate, thereby meeting the limitations of the claim. Because of the express definition for "systemically" in the specification, the Examiner's proposed interpretation for claim 2, that merely stopping blood flow is decreasing the flow rate, cannot be sustained because the flow rate is not shown to have been "systematically decreasing" as required by claims 1 and 2. Claim 11 further recites a method comprising the step of "systemically varying" the removal flow rate, which the Examiner has not interpreted according to the express definitions of the specification. Accordingly, these claims also are not anticipated by Holmes and the rejections should be withdrawn.

Claim Rejections – 35 USC §103

The Examiner rejects claims 3-10, 23, 24 and 28-39 under 35 USC §103(a) as being obvious over U.S. Patent 6,179,801 (Holmes et al.). These claims further clarify aspects of "systemically varying" the return flow rate and removal flow rate. Claims 4-7, 30-31 and 34-39 require the flow rates to meet specific equations, which are not taught or suggested in the prior art.

Incorporating the limitations of preceding claims, dependent claims 3, 8 and 9 recite a method of using total blood volume to determine the return and removal flow rate and decreasing the return flow rate in a substantially linear, exponential, or substantially exponential manner. The Examiner has rejected claims 3, 8 and 9 stating that Holmes teaches that the volume transfer rate of blood flow is variable based on a predetermined protocol of the apheresis machine. The Examiner regards this flow rate as a result-effective variable, the optimization of which involves only routine skill in the art (MPEP 2144.05). The Examiner considers the flow rates in the claims to be a result-effective variable that can be controlled by collected and calculated patient data, which is disclosed in Holmes. The Examiner similarly rejects claims 4-7, 24 and 28-39 as requiring optimizing a result-effective variable found in the prior art.

As presented above, Holmes does not disclose using total blood volume of the donor to adjust the return rate or removal rate of blood. MPEP 2144.05, relied upon by the Examiner, requires that:

"A particular parameter must first be recognized as a result effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of such variable might be characterized as routine experimentation. In re Antoine, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq.ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.)"

The Examiner has not established the fundamental premise for invoking this rule against Applicants' claims. One cannot logically arrive from the premise that donor blood volume may be used for some undisclosed purpose (Holmes, column 56, lines 61-67) to the conclusion that donor blood volume should be used for all purposes, such as adjusting removal rate and return rate of blood as proposed by the Examiner. The prior art has not recognized that return flow rate and removal flow rate can be beneficially varied according to total blood volume of the donor. These claims, therefore, should also be allowed. Furthermore, the specification provides results, which are not taught or suggested in Holmes, that the claimed methods demonstrate improvement in performance over the prior art (see the specification on page 31, line 16, through page 32, line 4). Accordingly, the obviousness rejections of claims 3-10, 23, 24 and 28-39 over Holmes should be withdrawn.

Additional claim limitations in claims 13, 16, 41, 46 and 51-68 are rejected under 35 USC §103 over Holmes and in view of U.S. 6,730,054 (Pierce et al.). Applicants believe these dependent claims are allowable with their parent claims for the reasons previously stated above. In addition, claims 55, 57-62 and 68 have further grounds for patentability.

Claims 54 and 55 address the maintenance of recirculated flow in the blood separation system, despite the fact that blood is alternatively being withdrawn from and returned to the donor. Claims 54 and 55 are amended to specify volumetric flow as assumed by the Examiner. As amended, the claims recite a method of blood processing having a recirculated component maintaining quasi-steady state flow conditions constant to within 10% of the volumetric flow. The Examiner states that Pierce discloses a blood processing system that recirculates a portion of PRP in a continuous fashion, where the entire volume is reintroduced to the first stage of the separation vessel. However, it has not been demonstrated that the Pierce device maintains the flow of blood within 10% of the volumetric flow as required by amended claim 54 and claim 55.

Because the blood processing device of the present invention is alternatively drawing blood from and returning blood to the donor, the flow of recirculated components must be varied to maintain constant conditions, such as volume, in the blood processing vessel. Thus the recirculation rate will be reduced during a blood draw phase and increased during a blood return phase. The quasi-steady state flow conditions are maintained in the separation system 115 and the collection lines 117, as described in the specification on page 23, lines 24-25, where the blood component separation takes place. Claim 54 is hereby amended to recite that the recirculated component maintains a quasi-steady state flow conditions in the separation system and the collection lines constant to within 10% of the volumetric flow.

In Pierce, the whole blood is separated into a red blood cell component and a platelet rich plasma (PRP) component. A portion of the PRP is then recirculated back into the separation vessel with whole blood (column 8, lines 53-60). Pierce does not disclose what amount this portion of PRP should be, or if the recirculated portion maintains a volumetric flow within 10%. Therefore, Pierce does not teach or suggest each and every claim limitation of claims 54 and 55.

Claims 57-62 and 68 recite specific hematocrit values and draw time and return time ratios for the recirculated blood component. The Examiner states that there is no teaching on control of hematocrit ratios in Pierce, but rejected claims 57 and 58 because Pierce generally suggests that the amount of recirculated blood is sufficient to establish desired conditions in the blood separation system. Thus, the Examiner considered the claim limitations of hematocrit control to be mere optimization of a result-effective variable. Similarly, the Examiner rejects claims 59-62 and 68 because the selection of variable parameters such as duration of the draw and return cycles are also mere optimization of a result-effective variable.

As discussed previously, MPEP 2144.05 is only applicable if the variable is recognized in the prior art as "result effective." The mere existence of a characteristic, such as hematocrit of blood, does not amount to recognition of that characteristic as being controlled to achieve a particular result. The Examiner has not established from the cited prior art that hematocrit was recognized as a factor for control of the efficacy of a blood separation device. The Examiner also has made no showing with respect to draw and return time ratios or draw and return flow ratios, beyond the assertion that these characterizations exist. Therefore, it is improper under MPEP 2144.05 to treat the claim limitations as mere optimization of result-effective variables.

Additionally, the claimed ratios provide a significant advantage over the prior art. Page 35, line 19, describes the importance of the duration of the duty cycle D (draw and return time ratio). A larger duty cycle corresponds to blood processing having a longer draw cycle than return cycle. In this instance less blood is recirculated through the system and increased blood fractions may be collected with less risk of contamination. Moreover, the relationship between the hematocrit and draw and return ratios is described on page 36 of the specification, lines 7-19, and Figure 4.

To establish a prima facie case of obviousness against a claim, all of the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180

USPQ 580 (CCPA 1974) and MPEP 2143.03. In light of the above arguments, each and every claim limitation is taught or suggested by Holmes or by Holmes in combination with Pierce. Accordingly, Applicant requests the rejections under 35 U.S.C. 103 be withdrawn.

Conclusion

It is believed that this response does not require the payment of fees. However, if this is incorrect, please charge any deficiency to Deposit Account No. 07-1969. If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

Respectfully submitted,
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